



Sialoblastoma of the submandibular gland: a distinct entity?

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Abstract

Sialoblastoma is a rare congenital malignant tumor of the salivary glands. A case of a submandibular sialoblastoma in a 1.5-year-old child is presented. A comparative analysis on 79 pediatric cases reported in the literature suggests a less aggressive behavior for submandibular sialoblastoma in comparison with other sites. Classically, diagnosis is confirmed by open biopsy, but fine-needle aspiration may offer an alternative with reduced morbidity. Expression of AFP and high levels of Ki-67 have been associated with poor prognosis. Whilst early surgical resection with negative margins is widely accepted as first-line treatment, there is no consensus on therapy of recurrence and follow-up. MRI and sonography represent valid tools for the follow-up, which is usually restricted to 3–5 years.

Conclusion: Submandibular sialoblastomas may have a different biological profile in comparison with parotid tumors with the absence of metastasis and much lower rate of recurrence. Comprehensive diagnostics should include additional options such as fine-needle aspiration and markers to assess cell proliferation and AFP. Literature suggests that surgery alone is sufficient for the treatment of tumors with low malignancy. Follow-up should be tailored according to the tumor site and might be limited to 3–5 years.

What is Known:

- *Sialoblastoma is a rare congenital malignant tumor with an unpredictable clinical outcome.*

What is New:

- *Sialoblastoma of submandibular origin seems to have a less aggressive behavior in comparison with other sites.*
- *Fine-needle aspiration and markers to assess proliferation index (i.e., suggestive of potential more aggressive course/malignancy) should be strongly considered in the diagnostic work-up.*
- *Radical surgery as first-line therapy and a 3–5-year follow-up are acceptable for tumors with a low malignancy.*

Keywords Sialoblastoma · Salivary gland · Children · Congenital tumor

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Introduction

Sialoblastoma is an extremely rare congenital malignant salivary gland tumor of epithelial origin. First described in 1966 as a distinct pathological entity, sialoblastoma has been reported under a variety of names before a retrospective review recognized the same identity of these tumors [11]. Sialoblastoma predominantly arises in the parotid gland with much fewer cases in the submandibular gland. Most cases occur in young children, although some rare adult cases are reported. Initially considered as a benign tumor, it is now classified as a malignant epithelial salivary gland neoplasm. A variability regarding diagnostic and therapeutic management exists due to its rarity and highly individual clinical behavior [2, 4]. Based on a case of a sialoblastoma of the right submandibular gland in a 1.5-year-old patient, a literature review was conducted. Evidence is presented to support subdivision of sialoblastomas according to their origin.

Methods

A case analysis is presented and a literature review was performed. PubMed and Researchgate search included the following keywords: Sialoblastoma and/or Embryoma and/or Congenital salivary mass for the years 1960–2018. Inclusion criteria were < 18 years, peer-reviewed. Exclusion criteria were age > 18 years, not peer-reviewed; language was not an exclusion criteria. Additional articles were identified from reviews of the reference lists. Single articles already listed in review publications were not cited separately.

Results

Case analysis

A feverish 1.5-year-old child presented to the Emergency Pediatric Department with a round, painful, and firm mass of 4 cm in diameter in the right submandibular region since 3 days. Based on ultrasound findings with suspicion of an enlarged lymph node and elevated infection parameters (CRP 100 mg/L, Lc $19 \times 10^9/L$), an antibiotic therapy was initiated for lymphadenitis colli. The mass did not regress after normalization of the infection parameters. Repeat sonography was inconclusive and a subsequent magnet-resonance-imaging (MRI) defined a T2 rich, T1 poor, extremely contrast avid formation of $3.0 \times 2.4 \times 2.6$ cm in the posterior tail of the submandibular gland (Fig. 1 (1–2)) with no pathologic lymph nodes. An excisional biopsy was performed with iatrogenic, temporary paresis of the mandibular branch of the facial nerve. Histologically, a tumor composed of cribriform glandular structures was found with interspersed fibrous

septa. The glandular cells were small with little cytoplasm and hyperchromatic nuclei; mucoid material was seen within the glandular spaces. A low proliferation index was observed. No perineural infiltration was observed. The histology was characteristic of a sialoblastoma of the submandibular gland (Fig. 1 (3–4)).

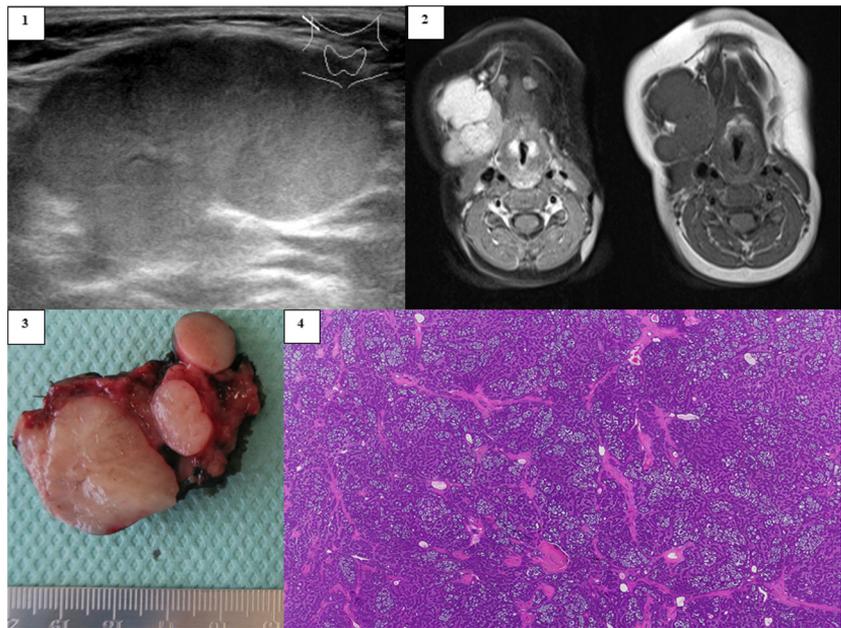
Staging was completed with a whole-body MRI in view of reported metastasis in lungs and bones for sialoblastoma and the Department of Otolaryngology was contacted. After discussion in the interdisciplinary tumor board, a tumor resection en bloc and a neck dissection of levels I to III of the right side under neuromonitoring were performed. The operation was uneventful; the mandibular branch of the facial nerve was visualized with postoperative incomplete paresis, which completely resolved after 4 weeks.

The pathologic examination confirmed a pT3 pN0 M0 pR0 pV0 sialoblastoma of the right submandibular gland, completely resected without fat or nerve infiltration. Consequently, there was no adjuvant treatment. A regular follow-up was performed including a 2-month clinical visit with neck-ultrasound, a 3-month MRI of the neck and skull-base in general anesthesia, and a 6-month lung CT-imaging. Thirty-six months after surgery, our patient proved disease-free by clinical examination and imaging.

Literature review

Sixty-seven original articles were retrieved from the search, of which 65, peer-reviewed, remained after exclusion/inclusion criteria; of them, 6 [1, 3, 6, 8, 9, 13] were not already listed in previous reviews [2, 4, 12]. Sialoblastoma seems to arise preferentially in the parotid glands in about 69.6% of the cases, less often in the submandibular gland (23.8%) and rarely in the minor salivary glands or other regions (Table 1). The classical clinical presentation in most cases was an indolent, slowly expanding cheek or submandibular mass. The onset was either congenital or early in childhood, less often in infants. Pattern of metastasis and recurrence were different depending on the origin. Metastasis was not seen in submandibular sialoblastoma and recurrence rate was different compared with the parotid site: 5.5% (1 case) versus 38.2% (21 cases). Recurrence occurred between 3 and 17 months post-excision, the majority (80%) around 12 months [4]. Distant metastasis only occurred in cases with parotid sialoblastomas at initial diagnosis time both in the lungs and bone, and after initial treatment in lungs and lymph nodes [2, 4, 12]. Radio- and/or chemotherapy has only been applied for parotid tumors. Classic radiotherapy was chosen in seven cases as a way either to control local recurrence or to provide a palliative treatment [4]. The number of tumors detected at other sites is very small and therefore any conclusion is difficult to draw. To date, only four reported cases died due to sialoblastoma, all of parotid origin [4, 12].

Fig. 1 (1) Sonography, a defined mass in the posterior submandibular region with increased echogenicity. (2) MRI, axial section: a T1 poor, T2 rich, contrast avid mass in the posterior tail of the right submandibular gland with a maximum size of 3 cm. (3) Macroscopic sample of the tumor showing a polylobulated shape. (4) Histology, cribriform glandular structures with interspersed fibrous septae and small glandular cells with little cytoplasm and hyperchromatic nuclei; mucoid material within the glandular spaces (magnification × 50)



Discussion

Pediatric sialoblastoma is a rare congenital malignant epithelial tumor of the salivary glands characterized by very individual courses [2, 4]. Submandibular tumors may have a

different biological profile in comparison with parotid tumors with the absence of metastasis and much lower rate of recurrence. Signal intensity seen on MRI—the radiologic imaging of choice—varies in the few available reports including this case and does not allow to predict aggressiveness of the tumor

Table 1 Characteristics of reported pediatric cases and comparison by original site; table based on literature search and quoted reviews

	Parotid	Submandibular	Other
Number of cases Total: 79	(55) 69.6%	(18) 23.8%	(6) 7.6%
Age			1 eyelid, 1 ectopic salivary tissue, 3 cheek, 1 minor salivary gland
Congenital	24 (43.6%)	11 (61.1%)	2 (34%)
Infant	11 (20%)	2 (11.1%)	1 (16%)
After first year	20 (36.4%)	5 (27.8%)	3 (50%)
Metastasis	9 (17.3%) (2 initial, 7 late) - Lung 7 - Lymph nodes 3 - Bone 1	None	None
Initial therapy	44 Parotid-/tumorectomy 8 Parotid-/tumorectomy neo-/adjuvant chemotherapy 2 Tumorectomy + radiotherapy 1 Neoadjuvant chemotherapy	13 Tumorectomy 5 Sialadenectomy	5 Tumorectomy 1 Tumorectomy + radiochemotherapy
Recurrence	21 (38.2%) within 3 to 17 months	1 (5.5%) after 1 month	1 (16%)
Follow-up	6–144 months	4–516 months	3–24 months
Therapy of recurrence	12 resection 3 resection + chemotherapy 1 Resection + radiochemotherapy 3 Chemotherapy 2 Chemotherapy and radiotherapy	1 resection	1 resection + neoadjuvant and adjuvant chemotherapy
Mortality	4 (7.3%)	0	0

[10]. There is some indication for immunostaining to be helpful for assessing grade of malignancy. Expression of AFP and high levels of Ki-67 have been associated with poor prognosis [2]. The low proliferation index in our patient would be in accordance with a better prognosis and confirmed by the absence of recurrence during available length of follow-up.

Classically, diagnosis is confirmed by open biopsy. However, associated morbidity of this approach, as seen in this case, is not to be neglected. Recently, fine-needle aspiration (FNA) and core needle biopsy have been applied with high sensitivity and specificity in the diagnosis of salivary gland tumors in adults, including one case of sialoblastoma in a child [5, 7]. Although some form of anesthesia must be administered in a child to perform FNA, considering the potential morbidity of open biopsy in young children, such as in this case, FNA could be a useful initial examination in childhood salivary masses.

While early surgical resection with negative margins is widely accepted as first-line treatment, there is no consensus of interval and length of follow-up. It is unclear if MRI represents the optimal choice for follow-up, as ultrasound might be a conclusive, cheap, and easily accessible alternative for older children. We employed MRI and ultrasound alternately (latter examination was feasible but with limited validity due to the patient's young age) and CT of the lungs. Neither recurrence nor metastasis has been seen in our case after 36 months. For submandibular tumors, follow-up imaging of the site of origin might be enough. As recurrence and/or metastasis have not been seen to occur later than 2 years after therapy, length of follow-up might be limited to 3–5 years. For recurrent disease, the preferential approach remains radical re-surgery, but in view of good outcome reports of chemotherapy, this option must be considered, especially in cases with high surgery-related morbidity [4, 12].

Conclusion

Sialoblastoma is a rare pediatric malignant epithelial salivary gland tumor of unknown origin that must be treated preferentially by surgery. Based on the literature review, we advocate separating parotid from submandibular site. The latter seems to be less aggressive with lower risk of recurrence and the absence of metastasis. FNA and immunohistological markers such as AFP and Ki67 should be included in the diagnostic work-up and might be helpful in evaluating malignant potential of the tumor. Both MRI and sonography represent valid tools for follow-up. For submandibular cases, local control seems to be enough.

Authors' contributions Authors' Contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by all authors. The first draft of the manuscript was written by Riccardo Di Micco and all authors commented on

previous versions of the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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